whether the teaching is provided through broad terminology or illustrative examples. *In re Wright*, 000 F.2d 1557, 1561 (Fed. Cir. 1993); *In re Marzocchi*, 439 F.2d 220, 223, 169 U.S.P.Q. 367, 369 (C.C.P.A. 1971). In *In re Brana*, 51 F3d 1560 34 USPQ2d 1436 at 1441 (1995), the court stated:

> [A] specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must* be taken as in compliance with the enabling requirement of the first paragraph of § 112 *unless* there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

> *In re Marzocchi*, 58 C.C.P.A. 1069, 439 F.2d 220, 223, 169 U.S.P.Q. (BNA) 367, 369 (CCPA 1971). From this it follows that the PTO has the initial burden of challenging a presumptively correct assertion of utility in the disclosure. *Id.* at 224, 169 U.S.P.Q. (BNA) at 370. Only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility. See *In re Bundy*, 642 F.2d 430, 433, 209 U.S.P.Q. (BNA) 48, 51 (CCPA 1981). [Emphasis in original. Footnote omitted.]

Applicant is not required to provide clinical data as if applying to the FDA for approval of a drug candidate; Applicants believe that the enablement requirement has been satisfied:

> Usefulness in patent law, and in particular in context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were [the court] to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer. [*Brana*, at 1442-1443.]

Furthermore, patent applicants preferably omit what is well known in the art. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987).

Applicants believe that the specification complies with the requirements 35 U.S.C.§ 112, first paragraph. Prodrugs are discussed on page 8, lines 12-23. Applicants request Examiner to reconsider and withdraw the rejection under 35 U.S.C.§ 112, first paragraph.

The Office Action states that claims 1-5, 7-10, and 13-26 are rejected under 35 U.S.C.§ 112, second paragraph as being indefinite. Each issue will be addressed separately and amendments made accordingly:

2(a) The Office Action states that the claims are rejected because of "C_{1-4} alky". "C_{1-4} alky" is a typographical error. In support of claiming that this is a typographical error, Applicants direct Examiner's attention to page 7, lines 14-18 for a discussion of C_{i-j}alkyl. This should read "C_{1-4} alkyl". Please add "l" after "C_{1-4} alky" to correct the typographical error:
page 5, line 6;
page 48, line 20.

2(b) The Office Action states that claim 1 is rejected, because of the period after "NH_2". "NH_2." at the end of the line on page 48, line 28 is a clerical error and should read "NH_2;". Please correct this typographical error on page 48, line 28 and on page 5, line 14.

2(c) The Office Action states that the claims are rejected because of the use of the word "Derivatives" and suggested using "Compound". Please delete "derivatives" and replace with "compound" on page 48, line 30.

2(d) and (e) The Office Action rejected claim 7 because it lacked "and" between the next-to-last species and last species and because claim 7 did not end with a period. Please place "and" before the last species in claim 7 on page 74, line 6. Please place a period at the end of claim 7 on page 74, line 8.

2(f) The Office Action rejected claim 8 because of the species "6-methyl1,2,3,4,5,5a,6,10b-octahydroazepino[4,5-b]indol-9-yl phenyl sulfone". Please add a "-" between "6-methyl" and "1,2,3,4,5,5a,6,10b-octahydroazepino[4,5-b]indol-9-yl phenyl sulfone". Page 74, line 10.

2(g) The Office Action rejected claims 13-26 for being vague an indefinite in that the claim provides for the use of claimed compounds, but the claim does not set forth any steps involved in determining which are the diseases capable of being mediated by modulation of the 5-HT receptor.

Determining whether a claim is definite requires an analysis of whether one skilled in the art would understand the bounds of the claim when read in light of the specification. *Solomon v. Kimberly-Clark Corp.* 216 F.3d 1372, 55 U.S.P.Q.2d 1279 (Fed. Cir. 2000) citing *Personalized Media Communications, LLC v. ITC*, 161 F.3d 696, 705, 48 U.S.P.Q.2d 1180, 1888 (Fed. Cir. 1998) (emphasis added). If the claims read in light of the specification reasonably apprise those skilled in the art of the scope of the invention, § 112 demands no more. *Id.* In other words, the definiteness of the claim language must be analyzed, not in a vacuum, but always in light of the teachings of the prior art and of the particular application disclosure as it would be interpreted by one possessing the ordinary level of skill in the pertinent art. *Solomon v. Kimberly-Clark Corp.* 216 F.3d 1372, 55 U.S.P.Q.2d 1279 (Fed. Cir. 2000) citing *In re Moore*, 439 F.2d 1232, 169 U.S.P.Q. 236 (CCPA 1971). Additionally, the claims should not be rejected for non-inclusion of additional limitations dealing with factors which must be presumed to be within the level of ordinary skill in the art; the claims need not recite such factors where one of ordinary skill in the art to whom the specification and claims are directed would consider them obvious. See *In re Skrivan*, 427 F.2d 801, 806, 166 U.S.P.Q. 85, 88 (C.C.P.A. 1970).

The Office Action states that undue experimentation will be necessary to determine whether a given disease responds or does not respond to such an inhibitor. Which diseases are implicated in the inhibition of 5-HT receptors or modulation thereof is within the knowledge of one of ordinary skill in the art. For example, the specification enumerates several diseases implicated in 5-HT modulation, and commonly available literature, such as The Merck Manual, by Merck Research Laboratories, (1999), enumerates various diseases known to implicate 5-HT receptors. In fact, serotonin receptors have been extensively studied and are the subject of reviews predating the filing date of the application. *See*, P.R. Saxena, "Serotonin receptors: subtypes, functional responses and therapeutic relevance," *Pharmac Ther.* Vol. 66, pp. 339-368 (1995).

Moreover, it is well known in the respective field that 5-HT ligands are effective in treating a wide range of central nervous system (CNS) disorders in particular, those listed in the specification and claims.

> Since the discovery of serotonin (5-hydroxytryptamine, 5-HT) over four decades ago, the cumulative results of many diverse studies have indicated that serotonin plays a significant role in the functioning of the mammalian body, both in the central nervous system and in peripheral systems as well. Morphological studies of the central nervous system have shown that serotonergic neurons, which originate in the brain stem, form a very diffuse system that projects to most areas of the brain and spinal cord. R. A. O'Brien, Serotonin in Mental Abnormalities, 1:41 (1978); H. W. M. Steinbusch, "Handbook of Chemical Neuroanatomy", Volume 3, Part II, 68 (1984); N. E. Anden, et al., Acta Physiologica Scandinavia, 67:313 (1966). These studies have been complemented by biochemical evidence that indicates large concentrations of 5-HT exists in the brain and spinal cord. H. W. M. Steinbusch, supra.
>
> With such a diffuse system, it is not surprising that 5-HT has been implicated as being involved in the expression of a number of behaviors, physiological responses, and diseases which originate in the central nervous system. These include such diverse areas as sleeping, eating, perceiving pain, controlling body temperature, controlling blood pressure, depression, schizophrenia, and other bodily states. R. W. Fuller, "Biology of Serotonergic Transmission", 21 (1982); D. J. Boullin, "Serotonin in Mental Abnormalities" 1:316 (1978); J. Barchas, et al., Serotonin and Behavior, (1973).
>
> Serotonin plays an important role in peripheral systems as well. For example, approximately 90% of the body's serotonin is found in the gastrointestinal system, and serotonin has been found to mediate a variety of contractile, secretory, and electrophysiologic effects in this system. Another example of a peripheral network that is very sensitive to serotonin is the cardiovascular system, which also contains its own source of serotonin, i.e., the platelet. Given the broad distribution of serotonin within the body, it is understandable that tremendous interest in drugs that affect serotonergic systems exists. In particular, receptor-specific agonists and antagonists are of interest for the treatment of a wide range of disorders, including anxiety, depression, hypertension, migraine, compulsive disorders, schizophrenia, autism, neurodegenerative disorders, such as Alzheimer's disease, Parkinsonism, and Huntington's chorea, and cancer chemotherapy-induced vomiting. M. D. Gershon, et al., "The Peripheral Actions of 5-Hydroxytryptamine", 246 (1989); P. R. Saxena, et al., Journal of Cardiovascular Pharmacology, 15:Supplement 7 (1990).

> Serotonin produces its effects on cellular physiology by binding to specialized receptors on the cell surface. It is now recognized that multiple types of receptors exist for all neurotransmitters and hormones, including serotonin. The existence of multiple, structurally distinct serotonin receptors has provided the possibility that subtype-selective pharmacologic agents can be produced. The development of such compounds could result in new and increasingly selective therapeutic agents with fewer side effects, since individual receptor subtypes may function to affect specific actions of the different parts of the central peripheral serotonergic systems. [US 5,698,444, filed December 23, 1993, issued December 16, 1997, Eli Lilly and Company as Assignee, col. 1.]

Therefore, claims 13-26 need not include factors obvious to one of ordinary skill in the art to whom the specification and claims are directed, especially when such an inclusion would be considered obvious and predates the filing date of the application. Consequently, claims 13-26 are definite to the extent necessary to achieve a complete exploration of Applicants' invention.

2(h) The Office Action rejected claim 20 stated that the phrase "e.g." rendered the claim indefinite. Please delete the parentheticals within claim 20.

Applicants have discovered a missing comma in claim 20. Please place a comma after "mood disorder" on page 75, line 14 of claim 20 as originally filed.

Applicant respectfully requests Examiner to reconsider all of the rejections based on 35. U.S.C.§ 112, and withdraw said rejections.

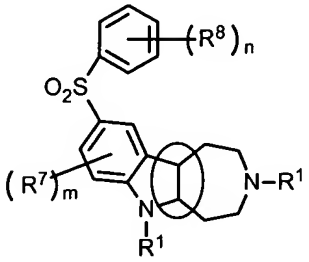
35 U.S.C. § 102(e)

Examiner rejects claims 1-7 and 13-26 as being anticipated by Jacobsen, et al., US Patent 6,468,999. The Office Action states that U.S. '999 teaches the compounds, compositions and method of use of the compounds of formula I where R^1 is H, Me, Et, isopropyl, etc.; R^7 is H; and R^8 is H, F, Me, OCF_3, OCH_3, -O-CH2-CH_2OH, etc., referencing examples 1-44. Applicants traverse.

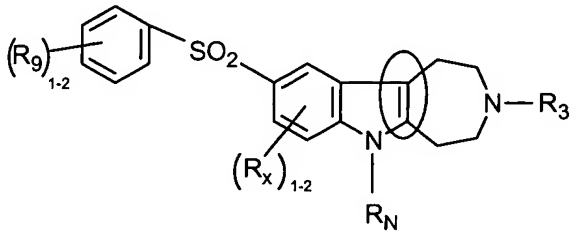
> "A claim is anticipated only if **each and every element** is set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegalal Bros. v. union oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed Cir. 1987). . . . . > "When a claim covers several structures of compositions, either generically or as alternatives, the claim is

deemed anticipated if any of the structures or compositions within the scope of the claim is known is the prior art." *Brown v. 3M*, 265 F.3d 1349, 1351, 60 USPQ2d 1375, 1376 (Fed. Cir. 2001) . . . . "The identical invention must be shown in as complete detail as is contained in the . . .claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). The elements must be arranged as required by the claim, but this is not an *ipsissimis verbis* test, i.e., identity of terminology is not required. *In re Bond*, 910 F.2d 831, 15 USPQ2d 1566 (Fed. Cir. 1990). . . . [MPEP, 2313.01, p 2100-70, Feb. 2003, emphasis added.]

U.S. '999 concerns 1,2,3,4,5,6-hexahydroazepino[4,5-b]indoles, their use, and intermediates thereof. The pending application concerns substituted indolines, their use, isotopically labeled compounds thereof, intermediates thereof and processes to make them. The claims in U.S. '999 do not anticipate the claims in the pending application, because indolines are different from indoles:



Formula I of pending application



Formula XII of US'999

Each and every element of the pending claim is not in U.S. '999, and, therefore, U.S. '999 cannot anticipate it. Applicants respectfully request Examiner to reconsider and withdraw the rejection.

35 U.S.C. §103

The Office Action states that claims 1-7 and 13-26 are rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent 6,468,999. It is also stated that: "The generic structure of U.S. '999 encompases the instantly claimed compounds (see Formula XII, column 1)", presented above. The Office Action claims that the substituents on the indoles and indolines "differ only in the nature of R_3, R_N, R_X and R_9." The Office Action also states: "Compounds of the instant invention are generically embraced by U.S. '999 in view of the interchangeability of the R_3, R_N, R_X and R_9 substituents on the tricyclic ring system. Thus, one of ordinary skill in the art at the time the invention was made would have been motivated to select for example benzyl as well as

other possibilities from the generically disclosed alternatives of the reference and in so doing obtain the instant compounds in view of the equivalency teachings outlined above." 6/10/03 Office Action, pages 7-8. Applicants respectfully traverse.

The rejection fails to acknowledge and address the fact that the core molecules are different: the pending application discloses indoles, while U.S. '999 discloses indolines. The compounds are different. Therefore, contrary to the Office Action, Examples 1-44 do not differ only in the nature of R_3, R_N, R_X and R_9, but also differ in the core molecule. The compounds in the pending application are indoles. The compounds in U.S. '999 are indolines. Applicants respectfully request Examiner to reconsider and withdraw the rejection.

Double Patenting Rejection

Under point 5, the Office Action states that claims 1-7 and 13-26 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-24 of U.S. Patent 6,468,999. Applicants traverse. The compounds in the pending application are indoles. The compounds in U.S. '999 are indolines. This difference between the compounds of the pending application and U.S. '999 make the compounds of the present application not embraced by the compounds of U.S. '999.

Under point 6, the Office Action states that claims 1, and 3-5 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 26 and 27 of co-pending Application No. 10/013,858. Applicants traverse.

Applicants do not believe that a terminal disclaimer is warranted in the pending application because the compounds of co-pending Application No. 10/013,858 concern indolines and the pending application concerns indoles. This difference between the compounds of the co-pending applications make the compounds of the present application not embraced by the compounds of the co-pending Application No. 10/013,858.

Furthermore, co-pending Application No. 10/013,858 is a divisional of US, '999, arising from a restriction requirement in Paper No. 5 in U.S. '999 (09/10/01 Office Action). U.S. '999 was filed 11 July 2000. The terminal disclaimer is for the later issuing case:

> If the "provisional" double patenting rejections in both applications are the only rejections remaining in those applications, the examiner should then withdraw that rejection in one of the applications (e.g., the application with the earlier filing date) and permit the application to issue as a patent. The examiner should maintain the double patenting rejection in the other application as a "provisional" double patenting rejection which will be converted into a double patenting rejection when the one application issues as a patent. [MPEP 804I.B. p 800-19, August 2001.]

Applicants respectfully request Examiner to reconsider and withdraw both double patenting rejections. However, if the rejections are not withdrawn, Applicants request Examiner to reconsider in which cases any disclaimer is required, because co-pending Application No. 10/013,858 is a divisional of US, '999, arising from a restriction requirement in Paper No. 5 in U.S. '999 (09/10/01 Office Action). U.S. '999 was filed 11 July 2000.

CONCLUSION

Accordingly, it is believed that claims are now in condition for allowance, early notice of which would be appreciated.

If any outstanding issues remain, Examiner is invited to telephone the undersigned to discuss the same. No fee is believed to be due for the submission of this response. Should any fees be required, please charge such fees or credit overpayment to Deposit Account No. 21-0718.

Respectfully submitted,

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